

REMARKS

Upon entry of the Amendment, claims 1-13 are all the claims pending in the application.

Preliminarily, Applicants respectfully request that the Examiner acknowledge Applicants' claim to foreign priority.

Claims 5-12 are withdrawn as being directed to non-elected claims.

The Abstract has been amended to overcome the objection. Support is found on page 1, lines 5-9 of the specification. No new matter has been added.

Claims 2 and 13 are amended. Support is found at page 16, lines 15-16 and page 3, line 7, respectively. No new matter has been added.

Claims 1 and 4 are amended to correct grammatical errors. No new matter has been added.

The abstract of the disclosure is objected to because it does not set forth an intended use.

In response, Applicants have amended the abstract to include an intended use. Therefore, it is respectfully requested that the objection be reconsidered and withdrawn.

Claim 13 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite.

In response, Applicants have amended claim 13 to define the variables of formula (7). As amended, claim 13 is clear and definite in accordance with § 112, ¶ 2. In view of the above, it is respectfully requested that the rejection be reconsidered and withdrawn.

Claims 2 and 3 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Weston (U.S. Patent 2,819,269).

In response, Applicants respectfully traverse the rejection as follows:

In regard to the assertion of anticipation by Weston, R1 in Weston is defined as a carboalkoxy group containing up to four carbon atoms inclusive in claim 1 at column 4, which means that the alkoxy group can have 1 to 3 carbon atoms. The specifically disclosed compound has a carboethoxy group on the piperazine nitrogen atom.

Therefore, a t-butoxy group is not contained in the disclosure of Weston. Thus, Weston does not anticipate claims 2 and 3 and it is respectfully requested that the rejection be reconsidered and withdrawn.

The Action alternatively continues and indicates that if the Weston genus is not anticipatory because it does not place the instant t-butyl ester described above in the public's possession, it is otherwise an obvious variant in view of the generic teaching to employ C1-C4 alkyl esters as set forth in claim 1.

Applicants respectfully do not agree because the broad generic teaching in Weston does not provide an enabling disclosure of Applicants' specifically claimed species. The nature of the invention is pharmacological, and lends itself to a high level of unpredictability. Little direction is provided in Weston and no specific working examples are provided. Thus, the disclosure of Weston would require undue experimentation to arrive at Applicants' invention. Weston does not render Applicants' invention novel and unobvious.

Claim 3 is not within the generic disclosure of Weston and is not an obvious variant. Therefore, it is respectfully requested that the rejection be reconsidered and withdrawn.

In addition, to expedite prosecution, Applicants have amended claim 2 to include the recitation, "wherein one optical isomer is present in excess to the enantiomer thereof," according

to page 16, lines 15-16 of the specification. Weston neither discloses nor suggests the optically active composition of Applicants' claims. Therefore, it is respectfully requested that the rejection be reconsidered and withdrawn.

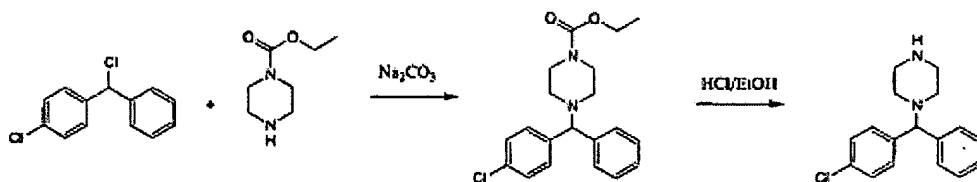
Claims 1, 4 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Weston in view of Cossement (U.S. Patent 5,478,941).

In response, Applicants respectfully traverse the rejection because Weston does not provide the basis for a *prima facie* obviousness rejection, even in combination with Cossement.

The structural differences in the cited art are too disparate for one skilled in the art to have been motivated at the time of Applicants' invention to have combined them.

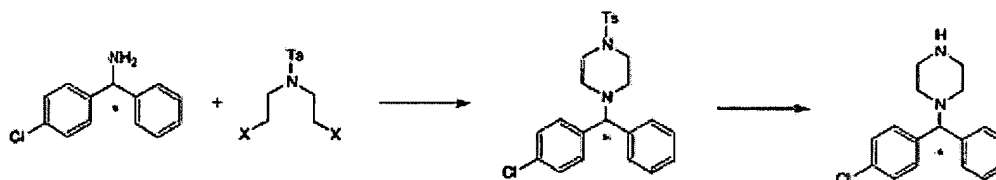
Weston teaches racemic N-(p-chlorobenzhydryl)-N-carbethoxypiperazine at column 2, but is silent on the optically active compound thereof or optical resolution. As one skilled in the art would appreciate, absent any indication how one would resolve the isomers, it would not be known how to isolate one enantiomer.

Weston teaches the following process in Example III on column 2:



Cossement only teaches optically active enantiomers of 1-[(4-chlorophenyl)phenylmethyl]piperazine of formula (IV) at column 4 and a process for producing the same by a process of reacting an enantiomer of (4-chlorophenyl)phenylmethylaniline of

formula (II) with N,N-diethyl-4-methylbenzensulfonamide of the formula (III) as outlined below:



Moreover, in view of the differences in the technical teachings of the references, one skilled in the art would not have been motivated to combine the teachings.

It is stated at lines 55-59, column 4 in Cossement that the compound of formula (III) is derived from nitrogen mustard. This statement would have served to discourage one of ordinary skill in the art from combining the references.

Applicants further traverse the obviousness rejection by pointing out the unexpected superiority of the claimed invention over the cited art.

The starting compound of the process of Cossement was prepared by optical resolution of the benzhydrylamine compound as disclosed in column 9 and then the tosylated compound was hydrolyzed using 4-hydroxybenzoic acid and 30% hydrobromic acid in acetic acid, as disclosed in Example 4 in column 10.

Removal of the tosyl group was conducted in a tedious manner, and the desired products were obtained in a yield of 84.8% as disclosed at line 42, column 10 and 78.6% at line 25, column 11.

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In the presently claimed process, as shown in Example 7, page 21, the removal of the t-butoxy group was accomplished quantitatively. Therefore, claim 13 is patentable because the process of Claim 13 provides unexpected results as compared with the teachings of Cossement.

The asserted references do not present a *prima facie* obviousness rejection, and further the claimed invention shows unexpected results that rebut any suggestion of obviousness. Therefore, it is respectfully requested that the rejection be reconsidered and withdrawn.

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

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